may be secondarily impetiginized and often spares areas of prior or active radiation. Tetracycline antibiotics, topical corticosteroids, and topical anti-acne treatments (such as benzoyl peroxide and clindamycin lotion) are helpful.

Several medications induce or exacerbate autoimmune disease. Interleukin (IL) 2, IFN-α, and anti-TNF-α are associated with new-onset systemic lupus erythematosus (SLE). Drug-induced lupus is classically marked by antinuclear and antihistone antibodies and, in some cases, anti-double-stranded DNA (D-penicillamine, anti-TNF-α) or p-ANCA (minocycline) antibodies. Minocycline and thiazide diuretics may exacerbate subacute SLE; pemphigus can be induced by D-penicillamine and ACE inhibitors. Furosemide is associated with drug-induced bullous pemphigoid. Vancomycin is associated with linear IgA bullous dermatitis, a transient blistering disorder.

Other medications may cause highly selective cutaneous reactions. Gadolinium contrast has been associated with nephrogenic systemic fibrosis, a condition of sclerosing skin with rare internal organ involvement; advanced renal compromise may be an important risk factor. Granulocyte colony-stimulating factor may induce various neutrophilic dermatoses, including Sweet syndrome and pyoderma gangrenosum. Both systemic and topical glucocorticoids cause a variety of atrophic skin changes, including atrophy and striae, and, in sufficiently high doses, can impede wound healing.

The hypothesis that a drug may be responsible should always be considered, especially in cases with atypical clinical presentation. Resolution of the cutaneous reaction may be delayed upon discontinuation of the medication (e.g., lichenoid drug eruptions may take years to resolve).

Photosensitivity Eruptions Photosensitivity eruptions are usually most marked in sun-exposed areas but may extend to sun-protected areas. The mechanism is almost always phototoxicity. Phototoxic reactions resemble sunburn and can occur with first exposure to a drug. Blistering may occur in drug-related pseudoporphyria, most commonly with NSAIDs (Fig. 74-1). The severity of the reactions depends on the tissue level of the drug, its efficiency as a photosensitizer, and the extent of exposure to the activating wavelengths of ultraviolet (UV) light (Chap. 75).

Common orally administered photosensitizing drugs include fluoroquinolones and tetracycline antibiotics. Other drugs less frequently encountered are chlorpromazine, thiazides, and NSAIDs. Voriconazole may result in severe photosensitivity, accelerated photo-induced aging, and cutaneous carcinogenesis in organ transplant recipients.

Because UV-A and visible light, which trigger these reactions, are not easily absorbed by nonopaque sunscreens and are transmitted through window glass, photosensitivity reactions may be difficult to block. Photosensitivity reactions abate with removal of either the drug or UV radiation, use of sunscreens that block UV-A light, and treating the reaction as one would a sunburn. Rarely, individuals develop persistent reactivity to light, necessitating long-term avoidance of sun exposure.

Pigmentation Changes Drugs, either systemic or topical, may cause a variety of pigmentary changes in the skin. Oral contraceptives may induce melasma. Long-term minocycline, pefloxacin, and amiodarone may cause blue-gray pigmentation. Phenothiazine, gold, and bismuth result in gray-brown pigmentation of sun-exposed areas. Numerous cancer chemotherapeutic agents may be associated with characteristic patterns of pigmentation (e.g., bleomycin, busulfan, daunorubicin, cyclophosphamide, hydroxyurea, and methotrexate). Clofazimine causes a drug-induced lipofuscinosis with characteristic red-brown coloration. Hyperpigmentation of the face, mucous membranes, and pretibial and subungual areas occurs with antimalarials. Quinacrine causes generalized, cutaneous yellow discoloration. Pigmentation changes may also occur in mucous membranes (busulfan, bismuth), conjunctiva (chlorpromazine, thioridazine, imipramine, clomipramine), nails (zidovudine, doxorubicin, cyclophosphamide, bleomycin, fluorouracil, hydroxyurea), hair, and teeth (tetracyclines).

Warfarin Necrosis of Skin This rare reaction (0.01–0.1%) usually occurs between the third and tenth days of therapy with warfarin, usually in women. Common sites are breasts, thighs, and buttocks (Fig. 74-2). Lesions are sharply demarcated, indurated, and erythematous or purpuric and may progress to form large, hemorrhagic bullae with eventual necrosis and slow-healing eschar formation. These lesions can be life threatening.

Development of the syndrome is unrelated to drug dose, and the course is not altered by discontinuation of the drug after onset of the eruption. Warfarin anticoagulation in heterozygous protein C deficiency causes a precipitous fall in circulating levels of protein C, permitting hypercoagulability and thrombosis in the cutaneous microvasculature, with consequent areas of necrosis. Heparin-induced necrosis may have clinically similar features but is probably due to heparin-induced platelet aggregation with subsequent occlusion of blood vessels; it can affect areas adjacent to the injection site or more distant sites if infused.

Warfarin-induced cutaneous necrosis is treated with vitamin K, heparin, surgical debridement, and intensive wound care. Treatment with protein C concentrates may also be helpful. Newer agents such as dabigatran etexilate may avoid warfarin necrosis in high-risk patients.

Drug-Induced Hair Disorders • ***DRUG-INDUCED HAIR LOSS*** Medications may affect hair follicles at two different phases of their growth cycle: anagen (growth) or telogen (resting). *Anagen effluvium* occurs within days of drug administration, especially with antimetabolite or other chemotherapeutic drugs. In contrast, in *telogen effluvium*, the delay is 2 to 4 months following initiation of a new medication. Both present as diffuse nonscarring alopecia most often reversible after discontinuation

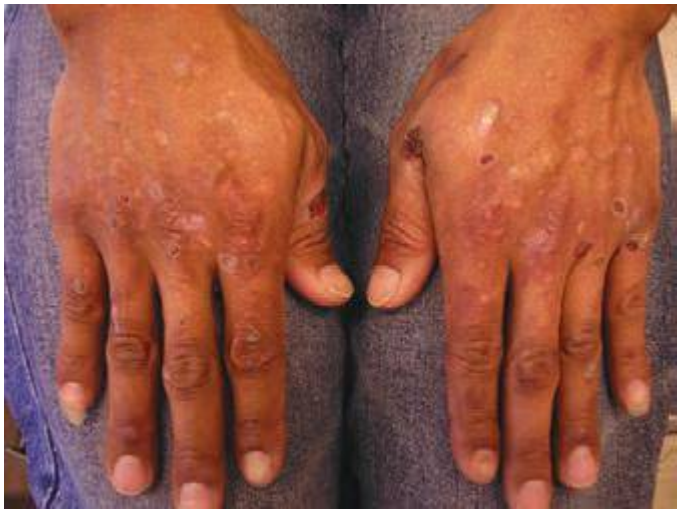

FIGURE 74-1 Pseudoporphyria due to nonsteroidal anti-inflammatory drugs.

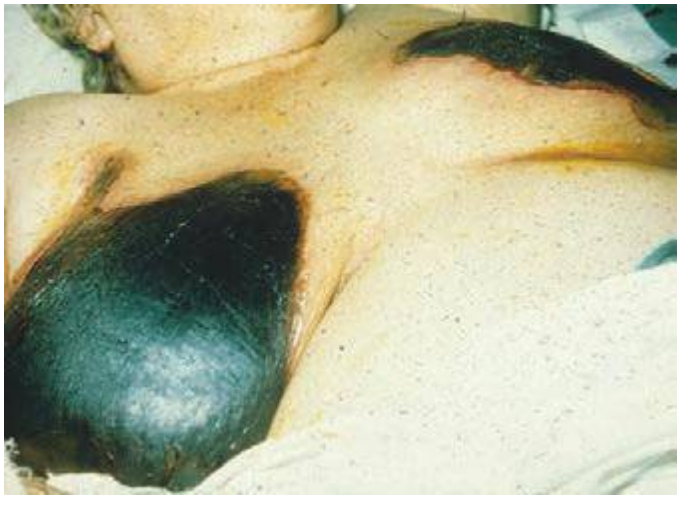

FIGURE 74-2 Warfarin necrosis.